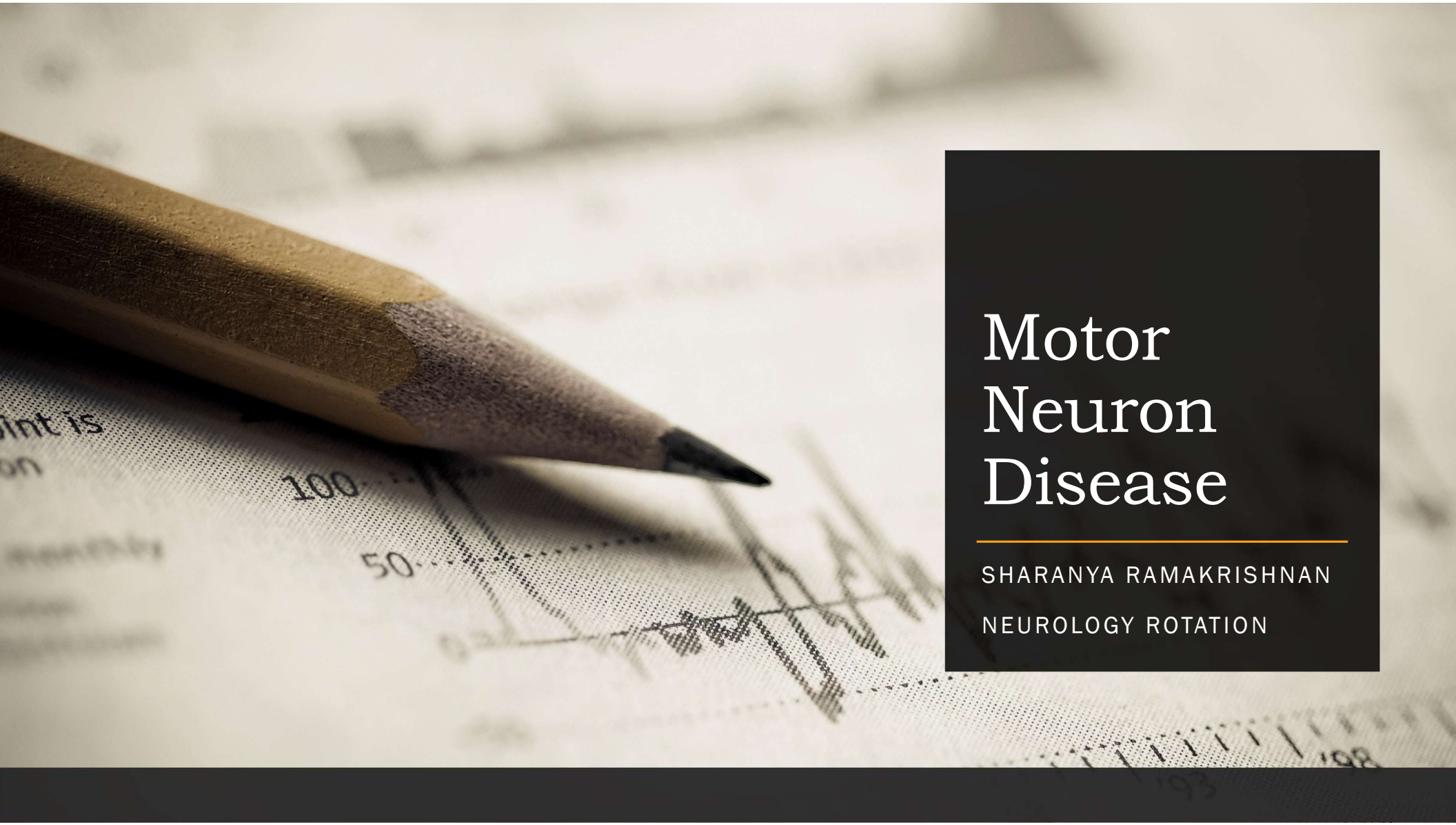

Motor Neuron Disease

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NEUROLOGY ROTATION

What is Motor Neuron Disease(MND)?

Includes a variety of inherited and acquired neurodegenerative conditions, that entirely or predominantly affect the motor system, with sensory sparing

1. Incidence of 2-3 in 100000, prevalence of 5-6 in 100000
2. Affects M>F, age 55–79; onset below 40 years is uncommon
3. Higher prevalence in Europeans/ European decent
4. Association between contact sports and sporadic cases (Lou Gehrig)
5. Association between low BMI and sporadic cases

Clinical presentations: Symptoms

- Isolated motor symptoms with sensory sparing.

Motor symptoms classification:

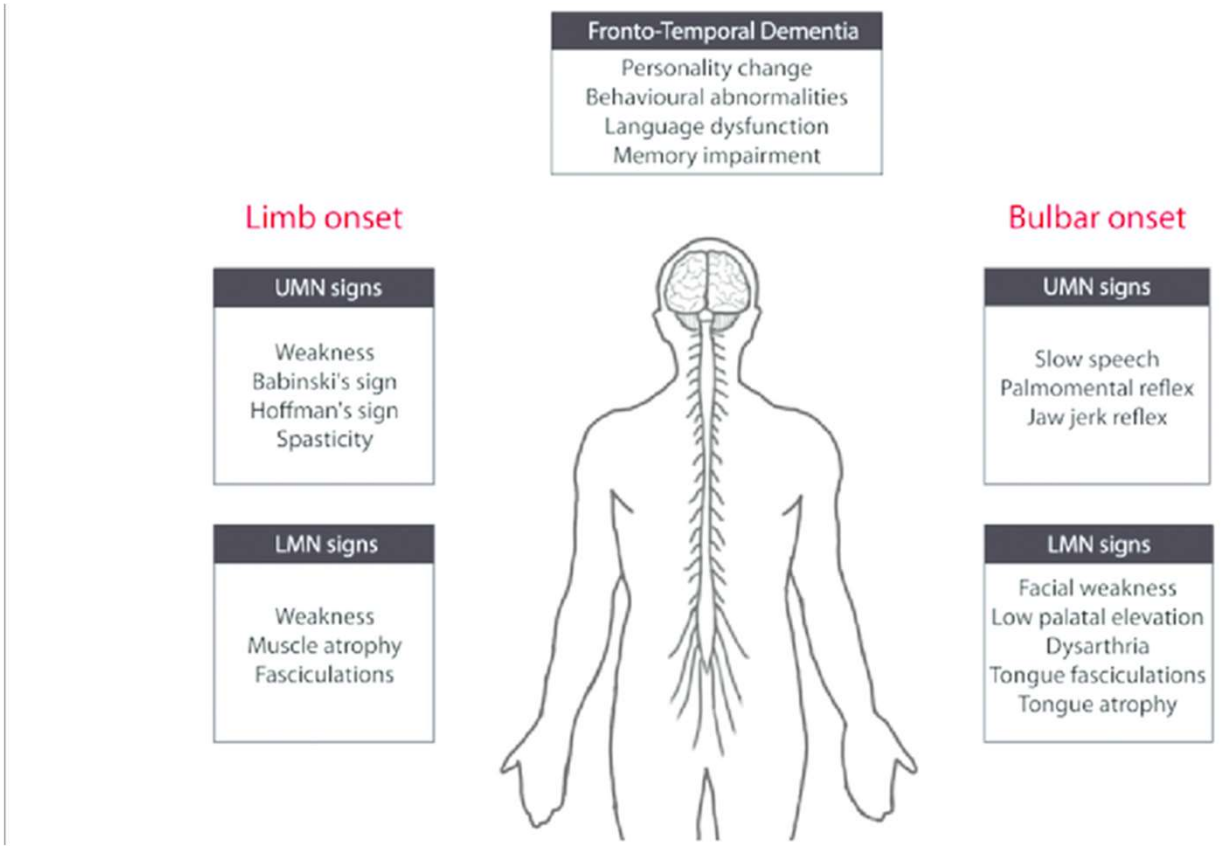
1. UMN symptoms
2. LMN symptoms
3. Mixed symptoms

Associated symptoms-

- Cognitive impairment: Many patients have some degree of cognitive impairment (35-50%). 10–15% of people with MND will show signs of frontotemporal dementia.
- Pseudobulbar affect: not specific (disruption of corticopontocerebellar pathway), 25-50% with MND affected. More common in primary lateral sclerosis and amyotrophic lateral sclerosis

-Excessive laughing, crying, yawning, not under voluntary control

Clinical presentation: General signs



Diagnosis of MND

1. Nerve conduction studies: preservation of sensory responses, normal or reduced motor amplitudes

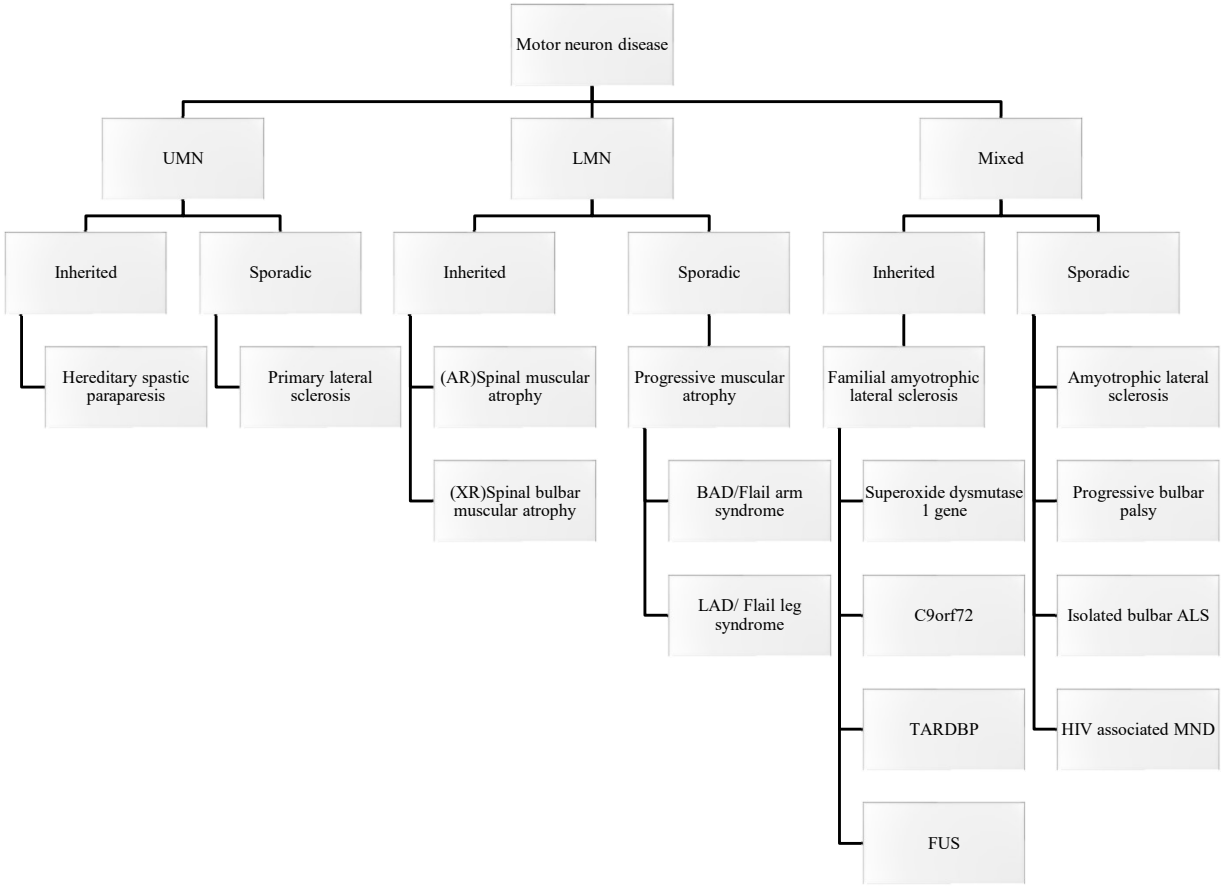
2. Needle EMG (Intramuscular): Will demonstrate

- Active denervation: Fibrillation potentials and chronic sharp waves
- Chronic denervation in multiple myotomes

3. MRI, Brain/Spine

-T2 weighted imaging- hyperintensity of corticospinal tract- Posterior limb of internal capsule, centrum semiovale,

Classification of Motor Neuron diseases



- *90% of all cases are sporadic while 10% are familial

MND Variants

1. Pure UMN variants:

A) Hereditary spastic paraparesis: (multiple inheritance pattens, 80) Familial, isolated lower limb spasticity

B) Primary lateral sclerosis: Sporadic, starts from the lower limbs- upwards, rarely early bulbar

2. Pure LMN variants:

A) Spinal muscular atrophy: (AR)

Type 1: Werdnig Hoffman: acute infantile

Type 2: chronic infantile

Type 3: Krugelberg-Welander: chronic juvenile

Type 4: Adult onset

B) Spinal bulbar muscular atrophy/ Kennedy's disease: (XR) Adult onset weakness: CAG repeats in androgen receptor gene

LMN symptoms proximal> distal + infertility + gynaecomastia

A) Primary muscular atrophy: Sporadic form, restricted to one spinal segment, but can gradually progress to ALS (Asymmetric proximal progresses to symmetric bilateral)

1) Brachial amyotrophic diplegia (BAD)/ Flail arm: restricted to cervical segment and longer life expectancy than ALS.

2) Leg amyotrophic diplegia/ Flail leg: Similar to flail arm, restricted to lower limbs

3. UMN+ LMN

A) Progressive bulbar palsy: Restricted to the bulbar region for a prolonged period, then progresses to ALS

B) Isolated bulbar palsy: Unlike progressive bulbar palsy, symptoms are solely restricted to bulbar region. Better prognosis than both ALS and progressive bulbar palsy.

Amyotrophic lateral sclerosis: Lou Gehrig's disease

- Mixed UMN+ LMN picture
- Both familial and sporadic variants exist. (Sporadic more common)
- Clinical symptom onset 50-70 years. Uncommon in <40years of age
- Clinical presentation: Mixed spasticity and weakness exists.

Objective assessment:

-Diagnosis by Revised El Escorial and Awaji criteria: **Definite ALS**: 3 spinal (UMN+LMN) *or* 2 spinal (UMN+ LMN) and 1 bulbar (UMN+LMN); **Probable ALS** 2 regions with UMN+LMN, with UMN being rostral to LMN or only 1 region clinically with UMN+LMN but 2 regions electrophysiologically; **Possible ALS** 1 region with UMN + LMN with LMN rostral to UMN *or* two regions with only LMN.

-Disability scoring by ALS-Milano Torino staging

-Cognitive assessment by ALS-Cognitive Behavioural screen

Clinical presentation: Specific signs

Split hand sign: Amyotrophic lateral sclerosis

(1st clinical sign)

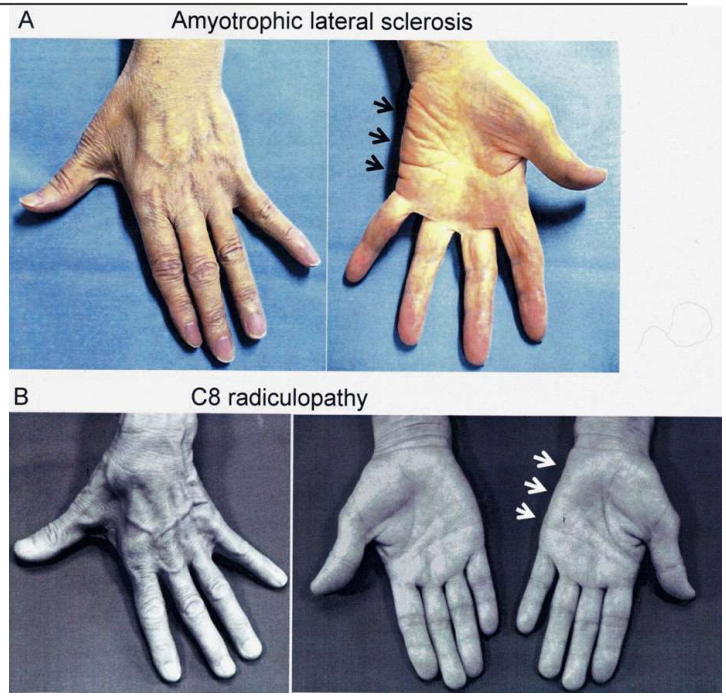
Atrophy of

1. 1st Dorsal interossei
2. Abductor pollicis brevis

(wasting of thenar eminence, but sparing of hypothenar eminence)

Differentiated from C8 radiculopathy by

1. Sensory involvement
2. Hypothenar wasting



Differential diagnosis: mimickers of ALS

Disorder	Differentiating test
Benign Fasciculations	No fasciculations/ recruitment of motor unit
Inclusion body myositis	Myopathic EMG, Muscle biopsy
Multifocal motor neuropathy	Nerve conduction studies with partial motor conduction block, anti-GM1 positive
Neuralgic amyotrophy (Parsonage Turner syndrome)	Very low amplitude of compound motor action potential
Monomelic amyotrophy (Hirayama disease)	MRI findings (lower cervical cord degenerataion and flattening, loss of attachment to dural sac, laminae)

Treatment

A) Pharmacological:

1. Riluzole (1990): Acts as a glutamatergic transmission inhibitor (Most widely used)- 3 month survival benefit

2. Edavarone (2017): Free radical scavenger. Speculation- Improved ALS Functional rating scale- Revised- by 33%

3. Symptomatic management of oral secretions, muscle spasms, psychiatric manifestations

For SMA specifically-

1. Nusinersin (2016): acts by increasing SMN protein, for better muscle function

2. Onasemnogeme abeparovec-xioi (Zolgensma): Gene replacement therapy on targeted motor neurons.

B) Non pharmacological: Depending on symptoms- (especially in bulbar involvement)

-Suction/early intubation

-Laryngeal muscle botulinum toxin/ bite guard/ hydration

Prognosis

- 50% survival after symptom onset was 2.5 years.
- Worse Prognosis if-

1. Bulbar onset of symptoms
2. Older age at diagnosis
3. Simultaneous arm/leg onset

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